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Review

Acute mesenteric ischaemia and unexpected death

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ABSTRACT

Acute mesenteric ischaemia is a vascular emergency that arises when blood flow to the intestine is compromised leading to tissue necrosis. It is primarily a condition of the elderly associated with significant morbidity and mortality. Causes include arterial thromboembolism, venous thrombosis and splanchnic vasoconstriction (so-called nonocclusive mesenteric ischaemia). Reperfusion injury and breakdown of the intestinal mucosal barrier lead to metabolic derangements, sepsis and death from multiorgan failure. The diagnosis may be difficult to make clinically and numbers of cases are increasing due to ageing of the population. The clinical and pathological features are reviewed with discussion of predisposing conditions. Careful dissection of the mesenteric vasculature is required at autopsy with appropriate histologic sampling and documentation of associated comorbidities. Other organs need to be checked for thrombi and the possibility of testing for inherited thombophilias should be considered. Toxicological evaluation, particularly in younger individuals, may reveal evidence of cocaine use. On occasion no obstructive lesions will be demonstrated, however the confounding effects of post-mortem autolytic and putrefactive changes may mean that nonocclusive mesenteric ischaemia may be difficult to diagnose.

1. Introduction

Reduction in blood flow to the intestine below the level required for normal metabolic functioning causes mesenteric ischaemia which may present acutely, or have a more chronic clinical progression. Acute mesenteric ischaemia is a vascular emergency that represents the end point for a variety of quite different, but sometimes overlapping, processes.[1] If blood flow is sufficiently compromised the result will be ischaemia leading to infarction of the intestines, a condition of the elderly that is associated with significant morbidity and mortality.[2] The clinical diagnosis is not always straightforward and cases are continually presenting to forensic facilities where the diagnosis had not been established prior to precipitate clinical decline and death. The term 'mesenteric ischaemia' is usually restricted to cases where there is an intrinsic abnormality of the vasculature and is differentiated from extrinsic mechanical compression of vessels due to distinct entities such as volvulus or herniation, although the terminal mechanisms in both include devitalization of the intestine with ischaemic necrosis and sepsis.[3,4]

The American Gastroenterological Association proposed three main categories of intestinal ischaemia to include acute mesenteric ischaemia, chronic mesenteric ischaemia (intestinal angina) and ischaemic colitis. Acute mesenteric ischaemia may be caused by arterial thromboembolism, venous thrombosis or splanchnic vasoconstriction (nonoclusive mesenteric ischaemia - NOMI).[5] The following paper provides an overview of the clinical and pathological features of acute mesenteric ischaemia, with discussion and illustration of some of the predisposing conditions.

2. Anatomy

The mesentery consists of a fold of peritoneum that suspends the small intestine from the posterior wall of the abdomen. It contains fat and supports blood and lymphatic vessels that connect to the intestine. The gut circulation accounts for a significant proportion of the cardiac output, receiving approximately 25% of the resting, and 35% of the post-prandial flow.[2]

The first major branch of the abdominal aorta, the coeliac artery, arises at the T12-L1 level and supplies foregut derivatives including the distal oesophagus, stomach and proximal duodenum. The next major aortic branch is the superior mesenteric artery which supplies midgut derivates extending from the distal duodenum, through the small intestine to the splenic flexure of the colon. Hindgut derivatives extending from the splenic flexure to the distal sigmoid colon are supplied by the inferior mesenteric artery.[6] The major branches all have collateral connections such as the pancreaticoduodenal arteries, the artery of Drummond and the arc of

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Riohan which can compensate to some degree if blood flow reduction is more chronic from, for example, gradual atherosclerotic narrowing.[7] This is usually not possible in cases of acute occlusion where there is dramatic reduction or cessation in blood flow. Seventy percent of the blood flow through mesenteric vessels supplies the mucosa and submucosa, with the remainder going to the muscularis and serosa.[2] This distribution explains the vulnerability of the intestinal lining cells to ischaemia.[8] Venous return from the gut is through the portal venous system of the liver.[9]

3. Classification and aetiology

The main reasons for significant fall in blood flow to the intestines are a reduction in arterial blood flow, or obstruction to venous return (Table 1). Arterial obstruction, most often involves the superior mesenteric artery, and occurs with embolisation from a cardiac lesion (40–50%), or from local thrombosis superimposed upon pre-existing stenosing atherosclerotic lesions (20–30%). Embolisation may be associated with atrial fibrillation, or recent myocardial infarction with mural thrombus formation. Emboli may also arise from valvular vegetations in bacterial endocarditis, and from mural thrombi associated with cardiomyopathies, ventricular aneurysms, valvular disorders or aortic aneurysms.[2,10] Paradoxical emboli are very rare.

Mesenteric arterial thrombosis due to atherosclerosis is usually a marker for more generalized atheromatous vasculopathy; for example, 70% of patients who have undergone an aortobifemoral bypass for stenosing atherosclerosis of the iliac arteries will have mesenteric arterial atherosclerosis.[11] In addition to atherosclerosis, thrombosis may be provoked by hypercoagulable states, hypovolaemia or shock.[9] Mesenteric vasculitis with superimposed thrombosis has also been reported in systemic lupus erythematosis,[12] although infarcts related to autoimmune conditions tend to be small and superficial.[8] Other rare causes of arterial thrombosis include dissections and aneurysms.

Venous thrombosis may be initiated by underlying sepsis, malignancy, major trauma, surgery, illness such as renal failure, systemic lupus erythematosus and maternal diabetes, and the prothrombotic states, or thrombophilias.[13] These include conditions where there are mutations in the factor V Leiden (causing activated protein C resistance) and prothrombin genes (*G20210A*), or deficiencies in anti-thrombin III, plasminogen, and proteins C and S, or antiphospholipid syndrome.[14] There is an increased risk of venous thrombosis with portal hypertension, chronic renal failure and congestive cardiac failure. Venous thrombosis is responsible for up to approximately 10% of cases of mesenteric ischaemia.[2]

Morbid obesity has been associated with an increase in risk for pulmonary thromboembolism. This is due not only to reduced mobility, but to a probable hypercoagulable state mediated by raised levels of fibrinogen, plasminogen activator inhibitor, factor VII, and factor VIII.[13] Obesity has also been shown to have a positive correlation with mesenteric venous thrombosis.[15] Certain autoimmune disorders also increase the risk of mesenteric venous thrombosis.[16]

Arterial blood flow may be non-obstructively reduced in cases of decreased flow to the peripheral splanchnic bed due to hypotension or to increased blood viscosity from dehydration or haematological disorders. Nonocclusive mesenteric ischaemia has been defined as “intestinal necrosis with a patent arterial tree” or “intestinal infarction without mesenteric vascular occlusion”.[1] There is a strong association with renal and cardiovascular disease, with the typical patient being over 60 years of age with diabetes, renal failure, hypertension dyslipidemia, atherosclerotic arterial occlusive disease, recent surgery and a history of smoking.[1,11] The exact aetiology is not understood however persistent and irreversible vasoconstriction are thought to play a role, mediated by angiotensin II and vasopressin from the kidney.[1] Vasoconstriction may also occur with a reduced cardiac output associated with other serious illnesses such as congestive cardiac failure.[17] It accounts for approximately 20% of cases of mesenteric ischaemia.[2]

Damage to intestinal tissues associated with mesenteric ischaemia is often due to reperfusion injury where decreased tissue oxygenation leads to an increase in microvascular permeability. If the period of ischaemia is prolonged the intestinal mucosal barrier breaks down under the influence of reactive oxygen metabolites

Table 1
Causes of acute mesenteric ischaemia.

Reduced arterial flow
Mesenteric arterial thrombosis
Mesenteric arterial thromboembolism
Atherosclerosis
Hypotension
Hypercoagulability
Arteritis
Vessel compression
Venous obstruction
Mesenteric venous thrombosis
Hypercoagulability
Vessel compression

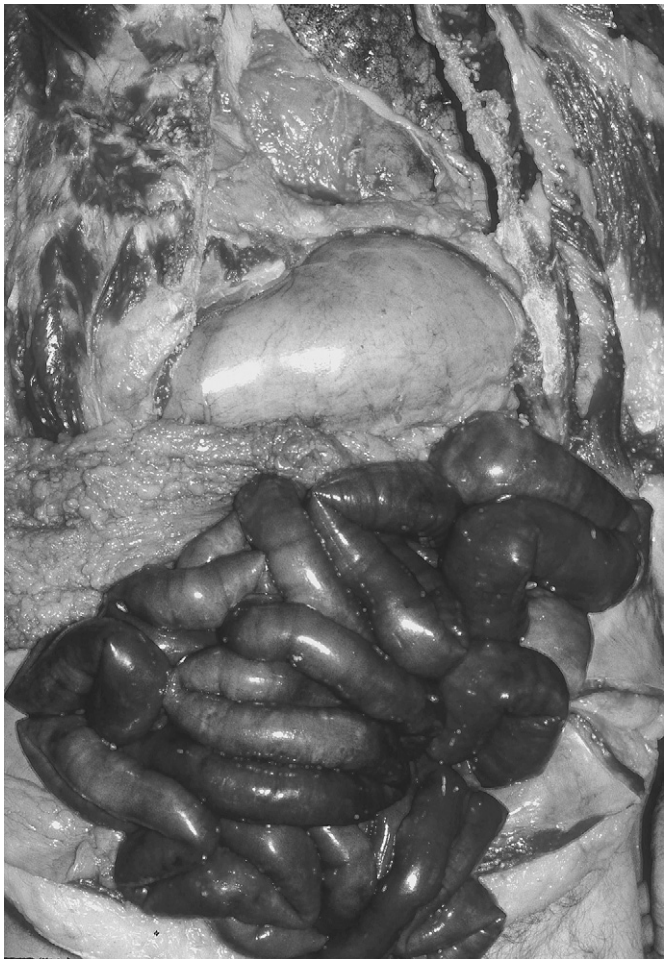

Fig. 1. Dark discolouration of the small intestine revealed on opening of the peritoneal cavity at autopsy in a 60-year-old man who died from infarction of the jejunum due to thromboembolic occlusion of the superior mesenteric artery.

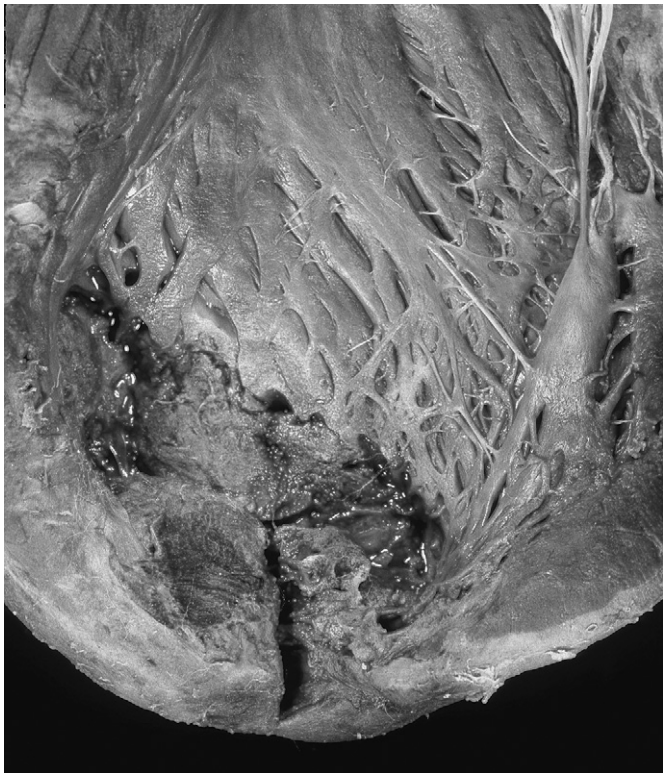

Fig. 2. Examination of the heart in the case from Fig. 1 showed the source of the embolus to be a large left ventricular mural thrombus overlying a recent myocardial infarct due to coronary artery thrombosis.

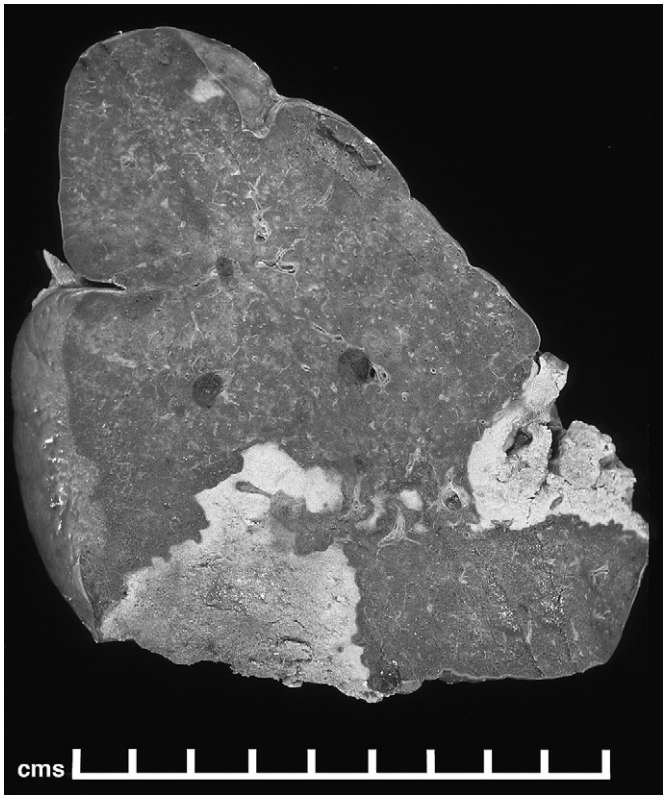

Fig. 3. Splenic infarction in a case of mesenteric ischaemia due to thromboembolism arising from mitral valve vegetations in a case of rheumatic heart disease.

and neutrophils. This results in intestinal necrosis with marked metabolic derangements, ileus, sepsis and death from multiorgan failure.[2]

4. Clinical presentation

The reported incidence of acute mesenteric ischaemia is increasing,[2,18] however, due to the non-specificity of clinical features the first indication of a mesenteric vascular lesion may be at autopsy in an elderly person who has been unwell for several days. The mortality rate has been reported up to 60–80%, although this depends on the underlying lesion, with venous thrombosis being much less lethal than either superior mesenteric artery thromboembolism or NOMI. The mortality rate of NOMI has been as high as 70–100%.[1] Acute ischaemia may have caused nausea, diarrhoea, blood from the rectum, vomiting or vague central abdominal pain.[18] The clinical finding of "pain out of proportion with physical findings" may be an indication in the history to suggest mesenteric ischaemia.[9] While acute arterial occlusion by a thromboembolus may produce the most striking clinical findings, more chronic atherosclerotic lesions may have been associated with so-called 'intestinal angina' with post-prandial pain, 'food fear'; and weight loss. Approximately one third of patients with an embolic lesion will have had a previous episode.[19] The features of venous thrombosis may also be quite subtle.[9] Associated complications of ileus, pancreatitis, peritonitis and gastrointestinal haemorrhage may have masked the clinical presentation with

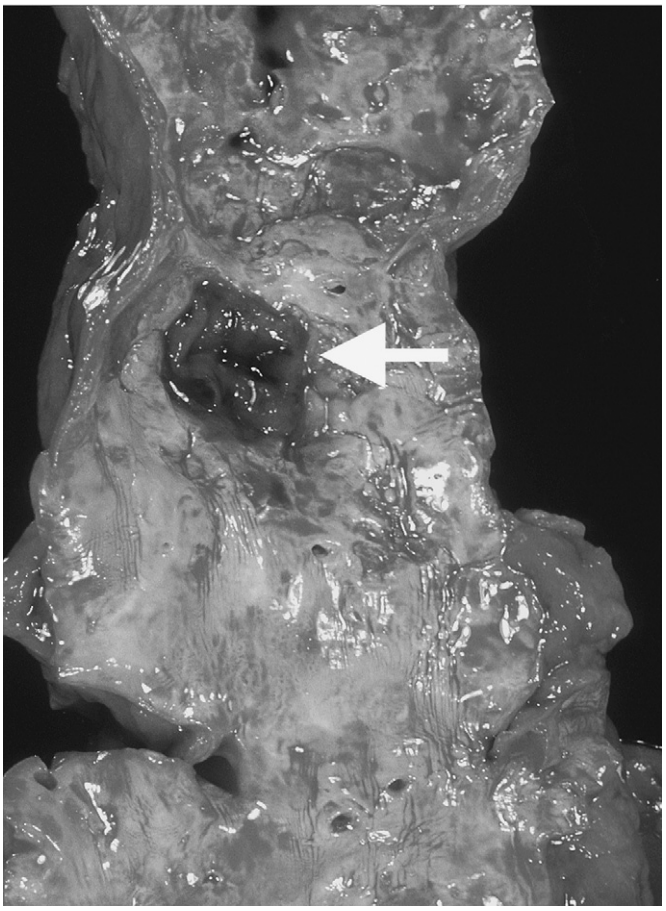

Fig. 4. Thrombotic occlusion of the proximal portion of the superior mesenteric artery and its ostium (arrow) in a 68-year-old man with hemiplegia, obstructive airways disease, heart failure and early pneumonia.

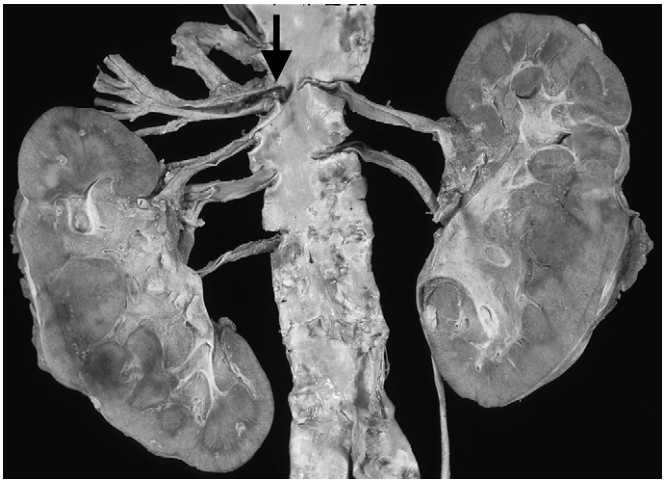

Fig. 5. Marked abdominal aortic atherosclerosis with superimposed thrombus in the proximal portion of the superior mesenteric artery (arrow).

disseminated sepsis and abdominal distension being late manifestations.[2] Reduction in mortality depends on early diagnosis and revascularization.[20]

In a six year clinical study of intestinal ischaemia the median age for patients with arterial embolism was 74 years (range 61–96) with the following associated conditions: atherosclerosis (90%),

Fig. 6. Opening of the superior mesenteric artery in a 75-year-old man with infarction of the entire small intestine, caecum and ascending colon showing distal propagation of the thrombus.

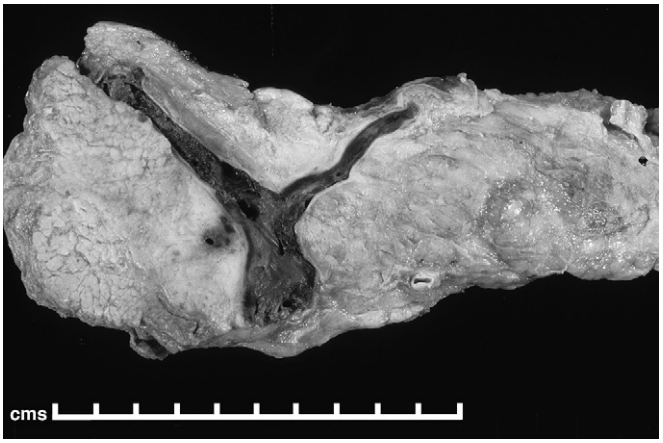

Fig. 7. Thrombosis of the superior mesenteric vein in a 63-year-old man with acute pancreatitis and peritonitis associated with portal venous thrombosis and thrombosis of veins draining the spleen and pancreas (pictured).

significant heart disease (85%) atrial fibrillation (75%), hypertension (85%), smoking (50%), digitalis use (50%) and obesity (40%).[21] This compared to patients with intestinal ischaemia from arterial thrombosis who were aged from 45 to 91 years (median 74 years) with the following conditions: atherosclerosis (89%), heart disease (79%), smoking (74%), hypertension (68%), cerebrovascular disease (47%), and obesity (42%).[21] If advanced atherosclerosis with superimposed thrombosis is found in younger individuals the possibility of an inherited disorder of lipid metabolism should be considered, or alternatively a local factor predisposing to accelerated atherogenesis such as previous radiotherapy for malignancy.[22] The possibility of drug effect should also be considered in the young, where chronic cocaine usage has been associated with accelerated atherogenesis and thrombosis of the superior mesenteric artery.[23] Finally, those with intestinal ischaemia from venous thrombosis tend to be younger, aged from 43 to 85 years (median 65 years), with the following: heart disease and atherosclerosis (62%), hypertension (67%), thrombophilic disorders (35%), chronic obstructive pulmonary disease (35%) and smoking (30%).[21]

5. Findings at autopsy

The first indication at autopsy will be of an ischaemic and/or infarcted appearance of the small intestine in the absence of

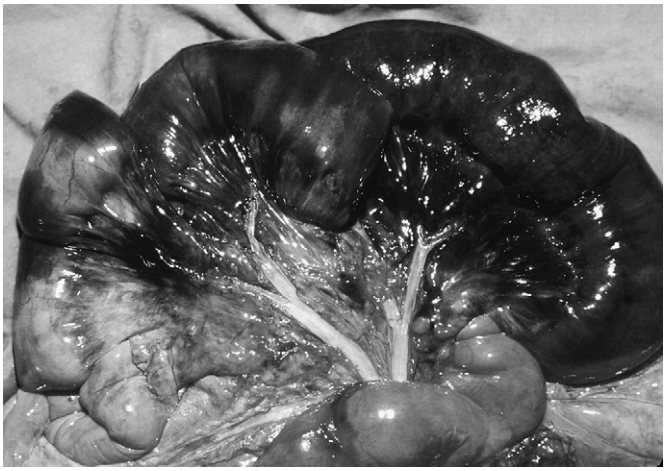

Fig. 8. Infarction of the jejunum with no obstructive lesions within the mesenteric vessels.

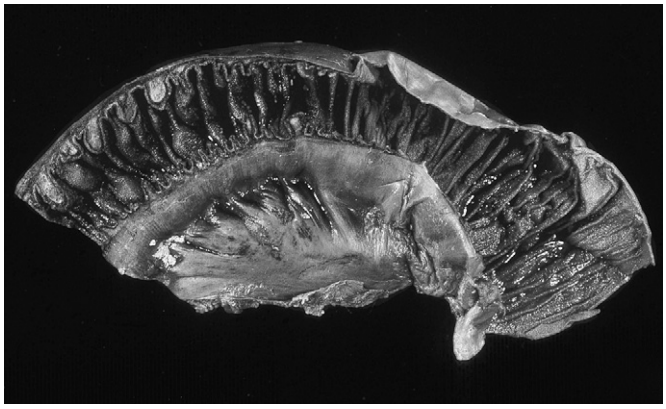

Fig. 9. Opened jejunum in the case from Fig. 7 demonstrating intense haemorrhagic infarction.

herniation or other mechanical reason for obstruction of blood flow. The loops of intestine will be plum coloured or gangrenous in appearance (Fig. 1). This finding should initiate a careful examination and dissection of the mesenteric vessels.

5.1. Arterial embolisation

Most emboli will be found within the superior mesenteric artery as its oblique angle of take-off from the aorta favours impaction. Dissection will most often reveal obstruction distal to the origin of the first main branch, the middle colic artery (50% of cases), with only 15% of emboli lodging at the origin.[2] The source of the embolus should be determined and associated lesions within the heart such as an acute myocardial infarct (Fig. 2) or ventricular aneurysm with mural thrombosis, endocarditis, rheumatic valve disease or cardiomyopathy, should be documented. There may be evidence of embolism with infarction in other tissues such as the kidneys and spleen (Fig. 3).

5.2. Arterial thrombosis

Mesenteric thrombosis usually also involves the superior mesenteric artery near its origin from the aorta in association with significant atherosclerosis (Figs. 4 and 5). Opening of the artery may reveal propagation of the thrombus distally (Fig. 6). Far less commonly there may be other causes of mesenteric arterial thombosis such as vasculitis associated with underlying systemic lupus erythematosus and so careful histologic sampling should be undertaken.[12] Thromboses tend to be associated with more extensive areas of intestinal infarction than those caused by embolism.[11] It should be recognized, however, that atherosclerotic narrowing of the mesenteric arteries is not uncommon, with 6–10% of the population having greater than 50% stenosis of at least one mesenteric artery identified at autopsy.[19]

5.3. Venous thrombosis

Mesenteric venous thombosis will be identified when dissection of the major mesenteric veins reveals antemortem thrombus. Thrombosis is usually segmental involving part of the superior mesenteric vein with haemorrhagic infarction of the attached intestine, although on occasion it may be more extensive (Fig. 7). The inferior mesenteric vein is far less often thrombosed.[2] Predisposing conditions, such as intra-abdominal malignancy, sepsis or pancreatitis, should be checked for, and the possibility of thrombosis elsewhere with or without an underlying thrombophilia should be considered.

5.4. Nonocclusive ischaemia (NOMI)

By definition, the finding of intestinal infarction, in the absence of mesenteric vascular occlusion, constitutes NOMI[1] (Figs. 8 and 9). Supportive features at autopsy include significant renal and cardiovascular disease.

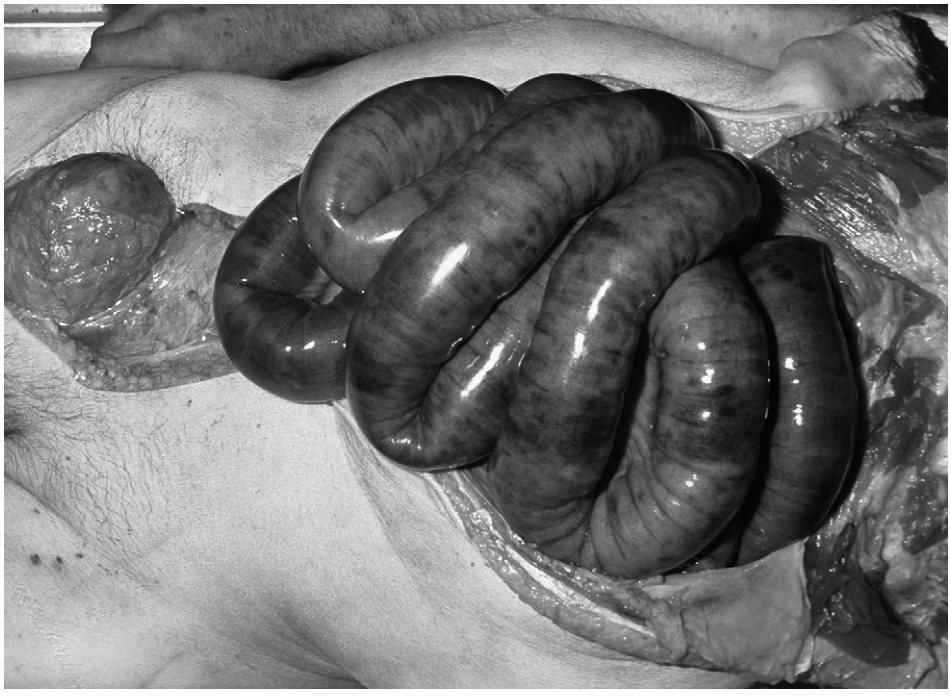

Fig. 10. Infarction of the small intestine revealed at autopsy.

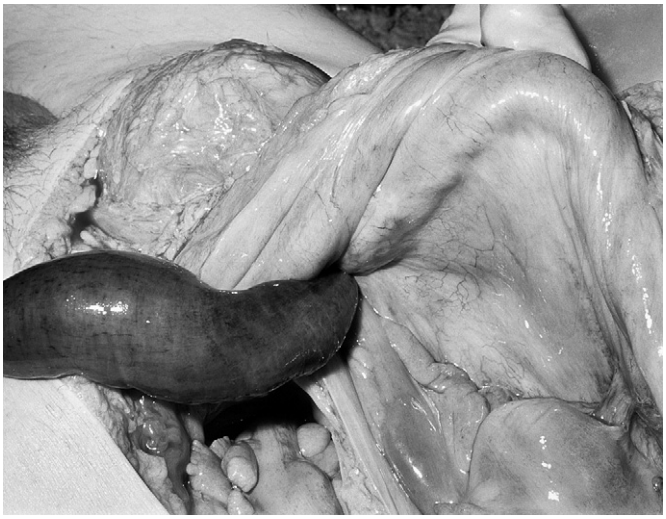

Fig. 11. Careful evaluation of the intestine *in situ* in the case from Fig. 10 showed the cause of the intestinal infarction to be a strangulated femoral hernia.

5.5. Miscellaneous

In certain cases of intestinal obstruction such as volvulus and herniation, there may be intestinal ischaemia resulting from external compression of mesenteric arteries and veins (Figs. 10 and 11). This may be associated with thrombosis. Coeliac axis compression, or Dunbar syndrome, refers to mesenteric ischaemia caused by compression of the vessel against the median arcuate ligament. It is a controversial entity that usually only manifests as episodic abdominal pain, weight loss and hyperemesis.[8,24]

In all of the above categories there should be careful histological sampling of multiple levels of the small intestine to clearly delineate any areas of ischaemic necrosis. In addition, cross-sections of the mesentery may identify arterial emboli or thombosis, venous thrombi, patent vessels or other pathology.

6. Conclusion

As acute mesenteric ischaemia may be a difficult diagnosis to make clinically, and as reported numbers are increasing due to the ageing population of many Western countries,[18] it is a condition that may be increasingly encountered in forensic practice. The approach to such cases requires the usual integration of the clinical history with the autopsy findings, in addition to careful dissection of the mesenteric vasculature with appropriate histologic sampling. Associated comorbidities need to be documented, and in the case of mesenteric venous thrombosis, other organs need to be checked for thrombi and the possibility of testing for inherited thombophilias should be considered. Toxicological evaluation, particularly in younger individuals, may reveal evidence of cocaine use. Cases will still be encountered where intestinal ischaemia is present but no obstructive lesions can be demonstrated (i.e. NOMI). The lack of clinical suspicions of intestinal infarction in NOMI,[17] the absence of obstructing vascular lesions at autopsy, and the confounding effects of post-mortem autolytic and putrefactive changes may mean that this particular subgroup of acute mesenteric ischaemia is most at risk of under-reporting at autopsy.

Conflict of interest

None declared.

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